(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 705 542 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
10.04.1996 Bulletin 1996/15

(51) Int Cl.[6]: **A23L 1/305**, A61K 31/195

(21) Application number: **95810580.1**

(22) Date of filing: **19.09.1995**

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

(30) Priority: **21.09.1994 US 309815**

(71) Applicant: **SANDOZ NUTRITION LTD.**
CH-3001 Berne (CH)

(72) Inventors:
- **Lowry, Carol J.**
  South Minneapolis, MN 55417 (US)
- **Schmidl, Mary K.**
  Arden Hills, MN 55112 (US)

(74) Representative: **Smolders, Walter et al**
Sandoz Technology LTD.,
Patents and Trademarks Division,
Lichtstrasse 35
CH-4002 Basle (CH)

(54) Adolescent dietary composition

(57) A dietary composition for oral or enteral administration to a human adolescent, comprising

a) a carbohydrate component which comprises from 50 to 65% of the total caloric content of said composition;

b) a lipid component which comprises from 20 to 35% of the total caloric content of said composition; and

c) an amino acid component which comprises from 10 to 20% of the total caloric content of said composition and which comprises 2.3 to 2.8 L-histidine, 6.1 to 7.4% L-isoleucine, 8.5 to 10.2% L-leucine, 7.0 to 8.4% L-valine, 6.6 to 8.0% L-lysine, 3.1 to 3.8% L-methionine, 5.5 to 6.6% L-phenylalaline, 4.8 to 5.8% L-threonine, 1.7 to 2.1% L-tryptophan, 5.7 to 6.9% L-alanine, 6.2 to 7.5% L-arginine, 5.9 to 7.1% L-aspartic acid, 2.3 to 2.8% L-cystine, 12.9 to 15.5% L-glutamine, 3.8 to 4.6% L-glutamic acid, 3.2 to 3.9% glycine, 5.0 to 6.0% L-proline, 5.4 to 6.5% L-serine, and 4.0 to 4.8% L-tyrosine, all based on total weight of said amino acid component.

EP 0 705 542 A1

Printed by Jouve (FR), 18, rue Saint-Denis, 75001 PARIS

Description

This invention relates to dietary compositions, useful for providing nutrition to a human adolescent, particularly in the age of 1 to 18 years, for stimulating growth or for diseases or conditions such as inflammatory bowel disease, intractable diarrhea, lactose intolerance, short bowel syndrome, cystic fibrosis, cow's milk protein enteropathy or sensitivity, pre or post surgery, AIDS, malabsorption syndrome, gastroenteritis, GI fistula, and pancreatic disorder.

BACKGROUND OF THE INVENTION

Providing proper nutrition to adolescents is important in growth and development. Nutrition is especially important to adolescents who are undergoing certain conditions or disease, and who are unable to consume food orally and must be fed enterally. Physicians have had to use baby formulas or modify existing adult enteral formulas to meet the needs of their adolescent patients. They have added fats and carbohydrates to increase the calories, lowered the protein content or reduced the water used in preparing powdered or concentrated varieties. These modifications do not provide for a well-balanced formula as the sodium and vitamins and minerals are not appropriate. Some physicians have added iron, vitamins and calcium, but again an appropriately balanced formula was not achieved. Thus, a strong need exists for improved enteral or oral formulas designed for the nutritional needs of adolescents.

Enteral food compositions containing essential amino acids, minerals and carbohydrates are described in U.S. patent no. 3,697,287. U.S. patent no. 4,368,204 describes elemental nutritional compositions for pediatrics having a specific amino acid profile. However, the compositions of the prior art are not optimal for providing nutrition to human adolescents. These compositions are typically too high in osmolality and relatively low in amount of essential amino acids and other components required for growth.

The present invention overcomes deficiencies of the prior art compositions by providing an improved nutritional composition for adolescents which has an optimal amino acid content.

DETAILED DESCRIPTION

The compositions of the invention comprise:

a) a carbohydrate component which comprises from 50 to 65% of the total caloric content of said composition;

b) a lipid component which comprises from 20 to 35% of the total caloric content of said composition; and

c) an amino acid component which comprises from 10 to 20% of the total caloric content of said composition and which comprises 2.3 to 2.8% L-histidine, 6.1 to 7.4% L-isoleucine, 8.5 to 10.2% L-leucine; 7.0 to 8.4% L-valine, 6.6 to 8.0% L-lysine, 3.1 to 3.8% L-methionine, 5.5 to 6.6% L-phenylalanine, 4.8 to 5.8% L-threonine; 1.7 to 2.1% L-tryptophan, 5.7 to 6.9% L-alanine, 6.2 to 7.5% L-arginine, 5.9 to 7.1% L-aspartic acid, 2.3 to 2.8% L-cystine, 12.9 to 15.5% L-glutamine, 3.8 to 4.6% L-glutamic acid, 3.2 to 3.9% glycine, 5.0 to 6.0% L-proline, 5.4 to 6.5% L-serine, and 4.0 to 4.8% L-tyrosine, all based on total weight of said amino acid component.

The carbohydrate component of the composition of this invention comprises 50-65% of the total caloric content of the composition, more preferably from 60 to 65% of the total caloric content; most preferably about 63% of the total caloric content. Any carbohydrate conventionally used in nutritional compositions are useful in the composition of this invention, but preferably the carbohydrate component consist essentially of maltodextrin, modified starch or mixtures thereof. The carbohydrate component provides optional absorption of the carbohydrate by the gastro-intestinal tract of adolescent, particularly for those with malabsorption disorders. The carbohydrate component more preferably consist essentially of about 72-99% by weight maltodextrin and about 1-28% by weight modified starch. The carbohydrate component is preferably free of lactose (which may be a problem in adolescents with lactose intolerance) and preferably contains no sucrose or fructose.

The lipid component for the compositions of this invention comprises from 20 to 35% of the total caloric content of the composition, more preferably 20 to 30%, most preferably about 25%. Adequate lipid intake is important as a source of energy, essential fatty acids and carrier of fat soluble vitamins. Suitable lipids for use in the present invention include, any of the conventional saturated and unsaturated fatty acids, glycerides and other nutritionally acceptable fat sources known in the art, such as animal oils, fish oils, vegetable oils and synthetic lipids. Preferably the lipid component consists essentially of soybean oil, medium chain triglycerides, or mixtures thereof. More preferably, the lipid component consists of about 30% by weight soybean oil and about 70% by weight medium chain, triglycerides, based on total weight of said lipid component. Medium chain triglycerides have been shown to be well-utilized in clinical conditions where standard long chain dietary fats are malabsorbed. In addition, medium chain triglycerides contain fatty acid chains composed of

six to ten linear carbon units. These triglycerides do not require emulsification with bile, are more rapidly and more easily hydrolyzed than long chain fats and the fatty acids are directly absorbed into the portal system. Soybean oil is preferred as an excellent source of linoleic and linolenic acids. The composition of the invention comprises preferably about 4.3% of its total energy content as linoleic acid and about 0.6% linolenic acid giving a total of about 4.9% as essential fatty acids.

The lipid component is preferably added or included in the compositions of the invention in the form of dry granules encapsulated by carbohydrate. The encapsulated lipid can be prepared by adding the lipid to an aqueous carbohydrate slurry, homogenizing it, and spray drying it to form the dry granules. The encapsulated lipid provides improved emulsion stability to the compositions of the invention.

The amino acid component of the compositions of this invention comprises from 10 to 20% of the total caloric content of the composition, more preferably 10 to 15%, most preferably about 12%. More preferably the amino acid component comprises 2.4 to 2.6% L-histidine, 6.6 to 6.8% L-isoleucine, 9.2 to 9.5% L-leucine, 7.6 to 7.8% L-valine, 7.1 to 7.4% L-lysine, 3.3 to 3.5% L-methionine, 6.0 to 6.2% L-phenylalanine, 5.2 to 5.4% L-threonine, 1.8 to 2.0% L-tryptophan, 6.2 to 6.4% L-alanine, 6.7 to 6.9% L-arginine, 6.4 to 6.6% L-aspartic acid, 2.4 to 2.6% L-cystine, 14.0 to 14.5% L-glutamine, 4.1 to 4.3 L-glutamic acid, 3.4 to 3.6% glycine, 5.4 to 4.6% L-proline, 5.8 to 6.1% L-serine, and 4.3 to 4.5% L-tyrosine, all based on total weight of said amino acid component. Most preferably the amino acid component comprises about 2.5% L-histidine, 6.7% L-isoleucine, 9.4% L-leucine, 7.7% L-valine, 7.3% L-lysine, 3.4% L-methionine, 6.1% L-phenylalanine, 5.3% L-threonine, 1.9% L-tryptophan, 6.3% L-alanine, 6.8% L-arginine, 6.5% L-aspartic acid, 2.5% L-cystine, 14.2% L-glutamine, 4.2% L-glutamic acid, 3.5% glycine, 5.5% L-proline, 5.9% L-serine, and 4.4% L-tyrosine, all based on total weight of said amino acid component.

The compositions of this invention preferably contain 100% free amino acids specially designed to provide a balance of amino acids for adolescents. This balance of amino acids is hypo-allergenic in comparison to intact protein used in other formulas. Free amino acids may have a unique benefit in the dietary management of adolescents sensitive to intact protein and for feeding adolescents with severe and persistent diarrhea. The amino acid profile of the present compositions meets or exceeds the standard for high quality proteins established by the National Academy of Science-National Research Council. The preferred non-protein calorie to nitrogen ratio to 200:1 and preferred total calorie to nitrogen ratio of 227:1 will meet the needs of adolescent patients. In general, protein requirements are increased during stress due to increased losses and greater needs for anabolism and tissue repair. Studies have shown the enteral fortification employing sufficient quantities of protein can accelerate the synthesis of visceral protein and promote positive nitrogen balance and host defense factors. However, excessive levels of protein are contra-indicated because of the resulting increase in renal solute load.

The amino acid component preferably comprises 9.5 to 11.5% by weight aromatic amino acid (such as phenlalanine and tyrosine) and 5.4 t 6.5% by weight sulfur-containing amino acids (such as methionine and cystine), based on total weight of the amino acid component. These are believed to be among the most important amino acids for growth in adolescents.

The compositions of the invention preferably contain L-carnitine and taurine. Adequate levels of L-carnitine are essential for lipid metabolism. The compositions preferably contain from about 0.01 to about 0.02% by weight based on total dry weight of the composition L-carnitine. Taurine is important for normal retinal development and in the synthesis of bile salts. Taurine also aids in improved fat absorption, growth and weight gain. The preferred compositions contain about 0.04 to 0.05% by weight taurine based on total dry weight of the composition.

The compositions of the invention can be in the form of a solid powder, this powder is subsequently dissolved or dispersed in juices, water or other aqueous based, non-protein medium. The solid powder form preferably has a caloric content from about 4-5 calories per gram of the composition. The compositions can also be in the form of a ready-to-use aqueous liquid which preferably has a caloric content of about 0.8 calorie per milliliter. The aqueous compositions of the invention preferably have an osmolality of about 300 to 400 mOsm per kilogram of water; more preferably about 350 to 370 mOsm/kg; most preferably about 360 mOsm/kg. Likewise, 0.22 grams of the dry powder composition in 1 gram of water has an osmolality of 300 to 400 mOsm.

Preferred compositions of the invention have the following formulation, based on total dry weight of the composition:

Ingredient	% by weight		
Maltodextrin	42.5960	to	52.0618
Modified starch	16.3556	to	19.9901
Medium chain triglycerides	7.5770	to	9.2608
Soybean oil	3.2834	to	4.0130
Calcium glycerophosphate	2.8007	to	3.4231
Magnesium gluconate	1.8886	to	2.3083
L-glutamine	1.4374	to	1.7568
L-lysine acetate	1.0375	to	1.2681
L-leucine	0.9471	to	1.1576
L-arginine acetate	0.9289	to	1.1354
Potassium Chloride	0.7879	to	0.9630
L-valine	0.7800	to	0.9533
Citric acid	0.7428	to	0.9079
L-isoleucine	0.6797	to	0.8307
L-aspartic acid	0.6574	to	0.8035
L-alanine	0.6351	to	0.7763
L-phenylalanine	0.6128	to	0.7490
L-serine	0.6017	to	0.7354
Polyglycerol ester	0.5669	to	0.6929
L-proline	0.5571	to	0.6809
L-threonine	0.5348	to	0.6537
L-tyrosine	0.4457	to	0.5448
L-glutamic acid	0.4234	to	0.5175
Potassium citrate	0.3580	to	0.4376
Glycine	0.3566	to	0.4358
L-histadine hydrochloride	0.3463	to	0.4233
L-methionine	0.3454	to	0.4222

Sodium citrate	0.2764	to	0.3378
L-cystine	0.2563	to	0.3132
Choline bitartrate	0.2386	to	0.2916
L-tryptophan	0.1894	to	0.2315
Sodium Phosphate dibasic	0.1818	to	0.2223
Potassium sorbate	0.1746	to	0.2134
Ascorbic acid	0.0938	to	0.1146
Alpha tocopheryl acetate	0.0836	to	0.1021
Beta carotene	0.0487	to	0.0595
Taurine	0.0415	to	0.0507
M-inositol	0.0338	to	0.0413
Zinc sulfate	0.0178	to	0.0218
Ferrous sulfate	0.0165	to	0.0201
Niacinamide	0.0133	to	0.0162
L-carnitine	0.0130	to	0.0158
Biotin	0.0065	to	0.0079
Copper gluconate	0.0047	to	0.0057
Calcium pantothenate	0.0037	to	0.0046
Vitamin A palmitate	0.0037	to	0.0045
Manganese sulfate	0.0033	to	0.0041
Vitamin D_3	0.0032	to	0.0040
Vitamin K_1	0.0025	to	0.0031
Cyanocobalamin	0.0020	to	0.0025
Potassium Iodide	0.0018	to	0.0021
Pyridoxine hydrochloride	0.0016	to	0.0020
Folic acid	0.0013	to	0.0016
Riboflavin	0.0012	to	0.0015
Thiamine hydrochloride	0.0010	to	0.0013
Chromic acetate monohydrate	0.00010	to	0.00011
Sodium molybdate	0.00010	to	0.00011
Sodium selenite anhydrous	0.000040	to	0.000044
TOTAL		**100**	

The most preferred composition comprises, based on total dry weight of the compositions:

Maltodextrin	47.3289
Modified starch	18.1728
Medium chain triglycerides	8.4189
Soybean oil	3.6482
Calcium glycero-phosphate	3.1119
Magnesium gluconate	2.0985
L-glutamine	1.5971
L-lysine acetate	1.1528
L-leucine	1.0524
L-arginine acetate	1.0321
Potassium Chloride	0.8755
L-valine	0.8667
Citric acid	0.8254
L-isoleucine	0.7552
L-aspartic acid	0.7305
L-alanine	0.7057
L-phenylalanine	0.6809
L-serine	0.6686
Polyglycerol ester	0.6299
L-proline	0.6190
L-threonine	0.5943
L-tyrosine	0.4952
L-glutamic acid	0.4705
Potassium citrate	0.3978
Glycine	0.3962
L-histidine hydrochloride	0.3848
L-methionine	0.3838
Sodium citrate	0.3071
L-cystine	0.2848

Choline bitartrate	0.2651
L-tryptophan	0.2105
Sodium Phosphate dibasic	0.2021
Potassium sorbate	0.1940
Ascorbic acid	0.1042
Alpha tocopheryl acetate	0.0929
Beta carotene	0.0541
Taurine	0.0461
M-inositol	0.0375
Zinc sulfate	0.0198
Ferrous sulfate	0.0183
Niacinamide	0.0147
L-carnitine	0.0144
Biotin	0.0072
Copper gluconate	0.0052
Calcium pantothenate	0.0042
Vitamin A palmitate	0.0041
Manganese sulfate	0.0037
Vitamin D_3	0.0036
Vitamin K_1	0.0028
Cyanocobalamin	0.0023
Potassium Iodide	0.0019
Pyridoxine hydrochloride	0.0018
Folic acid	0.0014
Riboflavin	0.0013
Thiamine hydrochloride	0.0012
Chromic acetate monohydrate	0.0001
Sodium molybdate	0.0001
Sodium selenite anhydrous	0.00004
TOTAL	**100**

The enteral nutritional compositions of this invention may be administered via a nasogastric, nasointestinal, esophagostomy, gastrostomy, or jejunostomy feeding tube. Because of its homogeneity and low viscosity, small bore feed-

ing tubes (16 gauge catheter or #5 French tube) may be used to optimize patient tolerance. The diet should be given at room temperature by continuous drip technique, or using a suitable infusion pump. At the 0.8 calorie per ml dilution, the composition supplies most of the daily fluid requirement. Additional fluids should be given when necessary to maintain hydration and adequate urine output.

The compositions can also be administered orally, such as a flavored drink served chilled over ice. The compositions of the invention are useful for administering complete nutrition or nutritional supplement to adolescents preferably ages 1 to 18 years, more preferably ages 1 to 10 years, most preferably ages 1 to 6 years. The compositions are preferably administered in an amount providing at least 800 calories per day. The compositions are particularly useful for administering to an adolescent for diseases on conditions such as inflammatory bowel disease, intractable diarrhea, lactose intolerance, short bowel syndrome, cystic fibrosis, cow's milk protein enteropathy or sensitivity, pre or post surgery, trauma, AIDS, malabsorption syndrome, gastroenteritis, GI fistula, and pancreatic disorder.

The following examples are presented to help demonstrate this invention. The examples are intended to be illustrative and not limitative.

EXAMPLE 1

A dietary composition (sample #8773) having an amino acid profile within the scope of the present invention was compared to a dietary composition containing casein as the standard protein source. These compositions had the following formulations:

Ingredients	Amount (wt. %)	
	Sample #8773	Casein Composition
Casein	-	11.14
Amino Acid Mix*	11.70	-
Cottonseed Oil	8.00	7.96
Vitamin Mix	1.00	1.00
Salt Mixture	5.00	4.81
Non-nutritive fiber	1.00	1.00
Corn starch	34.15	34.15
Sucrose	34.15	35.59
Water	5.00	4.35

* The Amino acid mix comprises:

Ingredient	% by weight
L-glutamine	12.2
L-leucine	8.0
L-arginine acetate	7.9
L-lysine acetate	8.8
L-isoleucine	5.8
L-valine	6.6
L-phenylalanine	5.2
L-methionine	2.9
L-threonine	4.5
L-tyrosine	3.8
L-histidine hydrochloride	2.9
L-aspartic acid	5.6
L-proline	4.7
L-tryptophan	1.6
L-serine	5.1
L-alanine	5.4
glycine	3.0
L-glutamic acid	3.6
L-cystine	2.2

The compositions were compared for Protein Efficiency Ratio (PER) which is a measure of protein quality using laboratory rats. PER is determined by dividing the animal's weight gain by protein intake. Two groups of ten rats each were fed a diet, for 28 days, of Sample #8773 and the casein composition, respectively. Every seven days the rats were weighed and their food consumption was recorded. At the end of 28 days, the total weight gain and protein consumption of the two groups were calculated. These values were used to calculate the PER.

The results for the casein composition are presented in Table 1 and in Table 2 for Sample #8773 of the invention.

Table 1
(Casein Composition)
BODY WEIGHTS - GMS
WEEKS

ANIMAL NUMBER	0	1	2	3	4	WT. GAIN
1	65	82	106	129	162	97
2	64	84	106	129	156	92
3	61	81	104	129	164	103
4	62	78	99	119	155	93
5	65	89	119	144	183	118
6	61	80	111	139	167	106
7	62	80	102	129	158	96
8	63	87	113	135	173	110
9	66	87	115	142	179	113
10	64	91	124	152	189	125
MEAN	**63**	**84**	**110**	**135**	**169**	**105**
SD	1.77	4.38	7.92	9.63	11.90	11.16

FEED CONSUMPTION - GMS

ANIMAL NUMBER	WEEKS 1	2	3	4	TOTAL	PROTEIN	PER*
1	69	97	96	98	360	36.0	2.69
2	75	88	96	95	354	35.4	2.60
3	69	86	89	103	347	34.7	2.97
4	72	81	87	114	354	35.4	2.63
5	81	101	109	121	412	41.2	2.86
6	73	96	109	106	384	38.4	2.76
7	74	84	101	112	371	37.1	2.59
8	80	89	94	116	379	37.9	2.90
9	78	98	102	120	398	39.8	2.84
10	85	107	113	129	434	43.4	2.88
MEAN	**76**	**93**	**100**	**111**	**379**	**37.9**	**2.77**
SD	5.30	8.33	8.77	10.81	28.28	2.83	.138

* PER = Protein Efficiency Ratio

TABLE 2 (SAMPLE #8773)

BODY WEIGHTS - GMS.

ANIMAL NUMBER	WEEKS 0	1	2	3	4	WT. GAIN
1	64	105	163	216	272	208
2	65	93	138	182	225	160
3	63	91	133	179	231	168
4	62	94	150	198	250	188
5	60	86	128	164	202	142
6	62	86	130	175	218	156
7	61	87	129	177	222	161
8	62	86	129	172	211	149

9	60	89	139	190	241	181
10	61	85	125	171	214	153
MEAN	**62**	**90**	**136**	**182**	**229**	**167**
SD	1.63	6.09	11.85	15.28	20.82	20.19

FEED CONSUMPTION - GMS
WEEKS

ANIMAL NUMBER	1	2	3	4	TOTAL	PROTEIN	PER
1	94	133	148	153	528	52.8	3.94
2	82	120	138	141	481	48.1	3.33
3	74	113	136	145	468	46.8	3.59
4	82	133	139	146	500	50.0	3.76
5	70	110	119	119	418	41.8	3.40
6	77	114	134	136	461	46.1	3.38
7	80	107	130	132	449	44.9	3.59
8	79	110	124	125	438	43.8	3.40
9	89	132	153	150	524	52.4	3.45
10	74	105	126	128	433	43.3	3.53
MEAN	**80**	**118**	**135**	**138**	**470**	**47.0**	**3.54**
SD	7.20	11.10	10.55	11.35	37.89	3.79	.191

The results show that compositions having the amino acid profile of this invention have a significantly greater protein efficiency ratio than the conventional casein protein.

EXAMPLE 2

A dietary composition within the scope of this invention (Sample A) was prepared and compared to a dietary composition described in U.S. Patent No. 4,368,204 (Sample B).

Sample A of this invention had the following composition:

Ingredient	% by weight
Maltodextrin	47.3289
Modified starch	18.1728
Medium chain triglycerides (MCT)	8.4189S
Soybean oil	3.6482
Calcium glycerophosphate	3.1119
Magnesium gluconate	2.0985
L-glutamine	1.5971
L-lysine acetate	1.1528
L-leucine	1.0524
L-arginine acetate	1.0321
Potassium Chloride	0.8755
L-valine	0.8667
Citric acid	0.8254
L-isoleucine	0.7552
L-aspartic acid	0.7305
L-alanine	0.7057
L-phenylalanine	0.6809
L-serine	0.6686
Polyglycerol ester	0.6299
L-proline	0.6190
L-threonine	0.5943
L-tyrosine	0.4952
L-glutamic acid	0.4705
Potassium citrate	0.3978

Glycine	0.3962
L-histidine hydrochloride chloride	0.3848
L-methionine	0.3838
Sodium citrate	0.3071
L-cystine	0.2848
Choline bitartrate	0.2651
L-tryptophan	0.2105
Sodium Phosphate dibasic	0.2021
Potassium sorbate	0.1940
Ascorbic acid	0.1042
Alpha tocopherylacetate	0.0929
Beta carotene	0.0541
Taurine	0.0461
M-inositol	0.0375
Zinc sulfate	0.0198
Ferrous sulfate	0.0183
Niacinamide	0.0147
L-carnitine	0.0144
Biotin	0.0072
Copper gluconate	0.0052
Calcium pantothenate	0.0042
Vitamin A palmitate	0.0041
Manganese sulfate	0.0037
Vitamin D_3	0.0036
Vitamin K_1	0.0028
Cyanocobalamin	0.0023
Potassium Iodide	0.0019
Pyridoxine hydrochloride	0.0018
Folic acid	0.0014
Riboflavin	0.0013
Thiamine hydrochloride	0.0012
Chromic acetate monohydrate	0.0001

Sodium molybdate	0.0001
Sodium selenite anhydrous	0.00004
Total	**100**

The caloric content of Sample A was 12% amino acid, 25% lipid and 63% carbohydrate. Comparative Sample B had the following composition:

Ingredient	% by wt.
Dextrin	82.40478
soybean oil	3.14522
L-leucine	1.31575
L-proline	1.27906
L-alanine	1.25809
L-lysine monohydrochloride	1.24367
L-serine	1.15718
L-glutamic acid	0.97895
L-arginine	0.90818
N-acetyl-L-tyrosine	0.70505
L-valine	0.70374
L-isoleucine	0.68015
L-threonine	0.65001
L-histidine hydrochloride	0.49799
L-cystine hydrochloride monohydrate	0.41019
L-phenylalanine	0.40626
di-L-aspartic acid monomagnesium	0.35842
L-aspartic acid monopotassium	0.35842
glycine	0.29749
Zinc sulfate heptahydrate	0.28137
L-tryptophan	0.24375

L-methionine	0.20837
potassium sorbate	0.15726
polysorbate 80	0.15412
ferrous gluconate	0.05762
choline bitatrate	0.03916
ascorbic acid	0.03748
soy lecithin	0.02202
vitamin K	0.01922
cupric sulfate pentahydrate	0.00180
tocopherol acetate	0.00722
Niacinamide	0.00481
Manganese sulfate pentahydrate	0.00285
Calcium pantothenate	0.00260
pyridoxine hydrochloride	0.00058
retinol acetate	0.00049
thiamine hydrochloride	0.00042
folic acid	0.00010
biotin	0.00009
riboflavine sodium phosphate	0.00006
ergocalciferol, D_2	0.00001
cyanocobalamin	0.000001
Total	**100**

The caloric content of Sample B was approximately 13% protein, 8% lipid and 79% carbohydrate.

Approximately 60-80 grams of Sample A and B, respectively, were dissolved in warm water to give 300 ml of solution. These solutions were prepared and visually evaluated by five individuals for instancy and solubility using a 5-point scale with 1=poor and 5=excellent. Instancy is defined as the amount of time with which the composition goes into solution and solubility is defined as quantity of insoluble particulates floating on the surface after the majority of the composition has gone into solution. The compositions were also visually evaluated for foaming, on the surface of the solution. The results of these evaluations are presented in Table 3.

TABLE 3

	Sample A (average rating)	Sample B (average rating)
Instancy	3.2	1.4
Solubility	2.6	1.8
Foaming	none	4 millimeters

Comparative Sample B exhibited lumps of product floating on the surface after mixing and there were no lumps of

product floating on the surface for Sample A of the invention. Comparative Sample B had a white particulate layer form on the bottom of the solution after sitting approximately 5 minutes whereas Sample A had no such sediment.

EXAMPLE 3

The composition of this invention, (Sample A) and the comparative composition (Sample B) prepared in Example 2 were rated for protein quality according to the Food and Agriculture Organization of the United Nations/ World Health Organization, Joint FAO/WHO Expert Consultation on Protein Quality Evaluation (1989), which is herein incorporated by reference. The compositions were given a score in comparison to egg having a score of 100 as the reference protein. The results of this scoring are presented in Table 4.

TABLE 4

		Sample A		Sample B	
Amino acid	Reference Protein (Egg) (mg/g)	Amino Acid value (mg/g)	% of Reference Protein	Amino Acid value (mg/g)	% of Ref. Protein
L-Histidine	22	23	105	24.3	110
L-Isoleucine	54	61	113	45	83
L-Leucine	86	85	99	87	101
L-Lysine	70	66	94	65.8	94
L-Methionine + L-cystine	57	54	95	32.5	57
L-Phenylal-anine + L-tyrosine	93	95	102	64.8	70
L-Threonine	47	48	102	43	91
L-Tryptophan	17	17	100	16.2	95
L-Valine	66	70	106	46.5	70
Chemical Score	100		94		57

This scoring shows that the essential amino acid component of the composition of the present invention is of higher quality than that of the comparative prior art composition. The scoring means that there is a limiting amino acid in the composition of this invention which is 94% of the egg reference protein, whereas the limiting amino acid of the comparative composition is only 57% of the egg reference protein.

Claims

1. A dietary composition for oral or enteral administration to a human adolescent, comprising

   a) a carbohydrate component which comprises from 50 to 65% of the total caloric content of said composition;

   b) a lipid component which comprises from 20 to 35% of the total caloric content of said composition; and

   c) an amino acid component which comprises from 10 to 20% of the total caloric content of said composition and which comprises 2.3 to 2.8 L-histidine, 6.1 to 7.4% L-isoleucine, 8.5 to 10.2% L-leucine, 7.0 to 8.4% L-valine, 6.6 to 8.0% L-lysine, 3.1 to 3.8% L-methionine, 5.5 to 6.6% L-phenylalanine, 4.8 to 5.8% L-threonine, 1.7 to 2.1% L-tryptophan, 5.7 to 6.9% L-alanine, 6.2 to 7.5% L-arginine, 5.9 to 7.1% L-aspartic acid, 2.3 to 2.8% L-cystine, 12.9 to 15.5% L-glutamine, 3.8 to 4.6% L-glutamic acid, 3.2 to 3.9% glycine, 5.0 to 6.0% L-proline, 5.4 to 6.5% L-serine, and 4.0 to 4.8% L-tyrosine, all based on total weight of said amino acid component.

2. The composition of claim 1 wherein said carbohydrate component comprises from 60 to 65% of the total caloric

content of said composition.

3. The composition of Claims 1 or 2, wherein said lipid component comprises from 20 to 30% of the total caloric content of said composition.

4. The composition of Claims 1 to 3, wherein said amino acid component comprises from 10 to 15% of the total caloric content of said composition.

5. The composition of Claims 1 to 4, wherein said amino acid component comprises 2.4 to 2.6% L-histidine, 6.6 to 6.8% L-isoleucine, 9.2 to 9.5% L-leucine, 7.6 to 7.8% L-valine, 7.1 to 7.4% L-lysine, 3.3 to 3.5% L-methionine, 6.0 to 6.2% L-phenylalanine, 5.2 to 5.4% L-threonine, 1.8 to 2.0% L-tryptophan, 6.2 to 6.4% L-alanine,6.7 to 6.9% L-arginine, 6.4 to 6.6% L-aspartic acid, 2.4 to 2.6% L-cystine, 14.0 to 14.5% L-glutamine, 4.1 to 4.3 L-glutamic acid, 3.4 to 3.6% glycine, 5.4 to 5.6% L-proline, 5.8 to 6.1% L-serine, and 4.3 to 4.5% L-tyrosine based on total weight of said amino acid component.

6. The composition of Claim 5 wherein said amino acid component comprises about 2.5% L-histidine, 6.7% L-isoleucine, 9.4% L-leucine, 7.7% L-valine, 7.3% L-lysine, 3.4% L-methonine, 6.1% L-phenylalanine, 5.3% L-threonine, 1.9% L-tryptophan, 6.3% L-alanine, 6.8% L-arginine, 6.5% L-aspartic acid, 2.5% L-cystine, 14.2% L-glutamine, 4.2% L-glutamic acid, 3.5% glycine, 5.5% L-proline, 5.9% L-serine, and 4.4% L-tyrosine based on total weight of said amino acid component.

7. The composition of Claims 1 to 6, wherein said carbohydrate component consists essentially of maltodextrin, modified starch or mixtures thereof.

8. The composition of Claims 1 to 7, wherein said lipid component consists essentially of soybean oil, medium chain triglycerides or mixtures thereof.

9. The composition of Claims 1 to 8, wherein said composition is in a dry powder form.

10. The composition of Claims 1 to 9, wherein said composition is dissolved or dispersed in a non-protein, aqueous-based medium.

11. The composition of Claim 10, wherein said composition has a caloric density of about 0.8 calories/ml and an osmolality of 300 to 400 mOsm/kg.

12. The composition of Claims 1 to 11, wherein 0.22 grams of said composition in 1 gram of water has an osmolality of 300 to 400 mOsm/kg.

13. The composition of Claims 1 to 12 comprising based on total dry weight of said composition:

Ingredient	% by weight		
Maltodextrin	42.5960	to	52.0618
Modified starch	16.3556	to	19.9901
Med.chain triglycerides	7.5770	to	9.2608
Soybean oil	3.2834	to	4.0130
Calcium glycerophosphate	2.8007	to	3.4231
Magnesium gluconate	1.8886	to	2.3083
L-glutamine	1.4374	to	1.7568
L-lysine acetate	1.0375	to	1.2681
L-leucine	0.9471	to	1.1576
L-arginine acetate	0.9289	to	1.1354
Potassium Chloride	0.7879	to	0.9630
L-valine	0.7800	to	0.9533
Citric acid	0.7428	to	0.9079
L-isoleucine	0.6797	to	0.8307
L-aspartic acid	0.6574	to	0.8035
L-alanine	0.6351	to	0.7763
L-phenylalanine	0.6128	to	0.7490
L-serine	0.6017	to	0.7354
Polyglycerol ester	0.5669	to	0.6929
L-proline	0.5571	to	0.6809
L-threonine	0.5348	to	0.6537
L-tyrosine	0.4457	to	0.5448
L-glutamic acid	0.4234	to	0.5175
Potassium citrate	0.3580	to	0.4376
Glycine	0.3566	to	0.4358
L-histidine hydrochloride	0.3463	to	0.4233
L-methionine	0.3454	to	0.4222

Sodium citrate	0.2764	to	0.3378
L-cystine	0.2563	to	0.3132
Choline bitartrate	0.2386	to	0.2916
L-tryptophan	0.1894	to	0.2315
Sodium Phosphate dibasic	0.1818	to	0.2223
Potassium sorbate	0.1746	to	0.2134
Ascorbic acid	0.0938	to	0.1146
Alpha tocopheryl acetate	0.0836	to	0.1021
Beta carotene	0.0487	to	0.0595
Taurine	0.0415	to	0.0507
M-inositol	0.0338	to	0.0413
Zinc sulfate	0.0178	to	0.0218
Ferrous sulfate	0.0165	to	0.0201
Niacinamide	0.0133	to	0.0162
L-carnitine	0.0130	to	0.0158
Biotin	0.0065	to	0.0079
Copper gluconate	0.0047	to	0.0057
Calcium pantothenate	0.0037	to	0.0046
Vitamin A palmitate	0.0037	to	0.0045
Manganese sulfate	0.0033	to	0.0041
Vitamin D_3	0.0032	to	0.0040
Vitamin K_1	0.0025	to	0.0031
Cyanocobalamin	0.0020	to	0.0025
Potassium Iodide	0.0018	to	0.0021
Pyridoxine hydrochloride	0.0016	to	0.0020
Folic acid	0.0013	to	0.0016
Riboflavin	0.0012	to	0.0015
Thiamine hydrochloride	0.0010	to	0.0013
Chromic acetate monohydrate	0.00010	to	0.00011
Sodium molybdate	0.00010	to	0.00011
Sodium selenite anhydrous	0.000040	to	0.000044
Total	**100**		

14. The composition of Claim 13 comprising, based on total dry weight of said composition:

Ingredient	% by weight
Maltodextrin	47.3289
Modified starch	18.1728
Medium chain triglycerides	8.4189
Soybean oil	3.6482
Calcium glycerophosphate	3.1119
Magnesium gluconate	2.0985
L-glutamine	1.5971
L-lysine acetate	1.1528
L-leucine	1.0524
L-arginine acetate	1.0321
Potassium Chloride	0.8755
L-valine	0.8667
Citric acid	0.8254
L-isoleucine	0.7552
L-asparic acid	0.7305
L-alanine	0.7057
L-phenylalanine	0.6809
L-serine	0.6686
Polyglycerol ester	0.6299
L-proline	0.6190
L-threonine	0.5943
L-tyrosine	0.4952
L-glutamic acid	0.4705
Potassium citrate	0.3978
Glycine	0.3962
L-histidine hydrochloride	0.3848
L-methionine	0.3838
Sodium citrate	0.3071

L-cystine	0.2848
Choline bitartrate	0.2651
L-tryptophan	0.2105
Sodium Phosphate dibasic	0.2021
Potassium sorbate	0.1940
Ascorbic acid	0.1042
Alpha tocopheryl acetate	0.0929
Beta carotene	0.0541
Taurine	0.0461
M-inositol	0.0375
Zinc sulfate	0.0198
Ferrous sulfate	0.0183
Niacinamide	0.0147
L-carnitine	0.0144
Biotin	0.0072
Copper gluconate	0.0052
Calcium pantothenate	0.0042
Vitamin A palmitate	0.0041
Manganese sulfate	0.0037
Vitamin D_3	0.0036
Vitamin K_1	0.0028
Cyanocobalamin	0.0023
Potassium Iodide	0.0019
Pyridoxine hydrochloride	0.0018
Folic acid	0.0014
Riboflavin	0.0013
Thiamine hydrochloride	0.0012
Chromic acetate monohydrate	0.0001
Sodium molybdate	0.0001
Sodium selenite anhydrous	0.00004
Total	**100**

15. The composition of Claims 1 to 14, wherein said amino acid component comprises from 5.4 to 6.5% by weight sulfur-containing amino acids.

16. The composition of Claims 1 to 15, wherein said amino acid component comprises 9.5 to 11.5% by weight aromatic amino acids.

17. The composition of Claims 1 to 16, wherein said lipid component is in the form of dry granules encapsulated by carbohydrate.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 95 81 0580

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	H.SCHERZ AND F.SENSER 'Food Compositions and Nutrition Tables 1989/90' 1989 , WISSENSCHAFTLICHE VERLAGSGESELLSCHAFT MBH , STUTTGART * page 124 - page 126 *	1-17	A23L1/305 A61K31/195
Y	EP-A-0 421 309 (SANDOZ NUTRITION LTD) 10 April 1991 * page 6 *	1-17	
Y	J. AM. DIET. ASSOC., 1994, vol. 94, no. 8, August 1994 pages 884-887, DUBIN S 'Essential amino acid reference profile affects the evaluation of enteral feeding products.' * page 885 *	1-17	
Y	DATABASE WPI Section Ch, Week 8649 Derwent Publications Ltd., London, GB; Class D13, AN 86-325130 & SU-A-1 228 844 (MOSC FIRST AID RES) , 30 April 1986 * abstract *	1-17	
A,D	EP-A-0 034 034 (AJINOMOTO KK) 19 August 1981 * claim 1 *		

TECHNICAL FIELDS SEARCHED (Int.Cl.6)
A23L
A61K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
MUNICH	11 January 1996	Bendl, E

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)